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EXAMINER	
WOODWARD, CHERIE MICHELLE	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,833	GIGER, ROMAN J.	
	Examiner	Art Unit	
	CHERIE M. WOODWARD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/24/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35,38-51 and 62-74* is/are pending in the application.

4a) Of the above claim(s) *1-35,42-49 and 62-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-41,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 October 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/31/06, 4/5/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group X (claims 36-41 and 50-51) in the reply filed on 24 September 2007 is acknowledged. Claims 36-37 and 52-61 have been cancelled by Applicant. Claims 1-35, 42-49, and 62-74 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 38-41 and 50-51 are under examination.

Information Disclosure Statement

2. The information disclosure statements (IDS) submitted on 31 October 2006 and 5 April 2007 have been fully considered. Signed copies are attached hereto. It is noted that a copy of the WO 03/018631 reference was not provided, but a copy of WO 03/038631 was found in Applicant's prior art document submissions of 10/31/2006. WO 03/038631 is drawn to a system and method for automated access of a network page and is not related to the instant invention. It appears that there was a mix-up in the WO numbers. The examiner was able to locate WO 03/018631 during the search and it was fully considered.

Drawings - Objection

3. The drawings are objected to because the cartoon of the chimera in Figure 12F-F" states that chimera "VI" consists of residues 1-346 of NgR1 and 328-420 of NgR2. However, the Brief Description of the Drawings (specification at page 6, paragraph 22, lines 26-27) states that the figure is supposed to represent residues 1-353 of NgR1 fused to residues 328-420 of NgR2. It is not clear whether the drawing or the description of the drawing correctly identifies the chimera of Figure 12F-F" (also listed as VI). If the drawing is not correct, corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either

"Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance. It is noted that the published WO 2004/090103 drawings and Brief Description

If the specification is not correct, then the specification should be amended to reflect the correct residues of NgR1 as taught in the drawings (see objection to specification below).

Specification - Objection

4. The disclosure is objected to because of the following informalities: the Brief Description of the Drawings (specification at page 6, paragraph 22, lines 26-27) states that the figure is supposed to represent residues 1-353 of NgR1 fused to residues 328-420 of NgR2. However, in the drawings, Figure 12F-F" states that chimera "VI" consists of residues 1-346 of NgR1 and 328-420 of NgR2. It is not clear whether the drawing or the description of the drawing correctly identifies the chimera of Figure 12F-F" (also listed as VI) (see Drawings objection, above).

There also appears to be a typographical error on page 7, line 2, in the Description of Figure 12(a), which refers to Figure "1c." There is no Figure 1c in the drawings. However, the description appears to correspond to Figure 12c.

Additional typographical errors include double parentheses on page 6 of the specification in lines 22 (12C""), 25 (12—E""), and 26 (12F-F""). There are no corresponding double parentheses in the corresponding drawings, only double primes (single parentheses).

Appropriate correction is required.

Claim Objections

5. Claim 39 is objected to under 37 CFR 1.821(d) because the recited amino acid residues to not recite an associated SEQ ID NO in the claim, as written. It is understood by the examiner that the recited amino acid sequence set forth in claim 39 is that of SEQ ID NO: 21. However, this is only set forth in the specification (p. 14, line 26). It must also be recited in the claim. 37 CRF 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application.

6. Claims 39 and 40 are objected to as being substantial duplicates. The chimera comprising amino acid residues 1-314 of NgR1, 315-327 of NgR2, and 354-473 of NgR1 (as recited in claim 39) is 100% identical to SEQ ID NO: 21 (recited in claim 40) (see specification p. 14, line 26). Both claim 39 and 40 are dependent on claim 38. SEQ ID NO: 21 is free of the prior art.

7. Claim 40 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. SEQ ID NO: 21 is free of the prior art.

Claim Rejections - 35 USC § 112, First Paragraph

Scope of Enablement

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 38, 41, 50 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for functionally active chimeras that bind MAG (myelin-associated glycoprotein), including chimeras comprising SEQ ID NO: 21, NgR2 (residues 315-420) [called "NgR2-unique"] fused to NgR1-LBD (residues 1-314), and NgR2-LBD (residues 1-315) fused to NgR1 (residues 313-473), does not reasonably provide enablement for the full scope of the genera of chimeras comprising NgR1 and the undefined "MAG binding motif" of NgR2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The level of skill of those in the art is in the area of molecular biology related to the construction of chimeric fusion proteins from known sequences.

The claims are drawn to a genus of chimeric NgR1 proteins comprising the "MAG binding motif" of NgR2; wherein the chimeric protein is soluble; a method of modulating myelin inhibitor activity comprising contacting a myelin-derived-inhibitor protein with the chimera; a method of treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of the chimera.

Barton et al., (EMBO J. 2003 Jul 1;22(13):3291-3302), teach that the myelin-derived proteins Nogo, MAG and OMgp limit axonal regeneration after injury of the spinal cord and brain (abstract). These cell-surface proteins signal through multi-subunit neuronal receptors that contain a common ligand-binding glycosylphosphatidylinositol-anchored subunit termed the Nogo-66 receptor (NgR) (abstract). Barton et al., teach that the binding of soluble fragments of Nogo, MAG and OMgp to cell-surface NgR requires the entire leucine-rich repeat (LRR) region of NgR, but not other portions of the protein (abstract). Despite sharing extensive sequence similarity with NgR, two related proteins, NgR2 and NgR3, do not bind Nogo, MAG, or OMgp (abstract).

He et al., (Neuron. 2003 Apr 24;38(2):177-185) teach that the failure of axon regeneration in the adult mammalian central nervous system (CNS) is at least partly due to inhibitory molecules associated with myelin (abstract). Recent studies suggest that an axon surface protein, the Nogo receptor (NgR), may play a role in this process through crossreactivity with myelin-associated inhibitory ligands (abstract). He et al., disclose the crystal structure and functional characterization of a soluble extracellular domain of the human Nogo receptor that provides a framework for structure-function studies aimed at assessing the physiological relevance of NgR-mediated protein-protein interactions to axon regeneration inhibition (abstract).

Domeniconi et al., (Neuron. 2002 Jul 18;35(2):283-90) teach myelin inhibitors of axonal regeneration, like Nogo and MAG, that block regrowth after injury to the adult CNS (abstract). MAG inhibits regeneration by interaction with NgR. Binding of and inhibition by MAG are lost if neuronal GPI-linked proteins are cleaved (abstract). Binding of MAG to NgR-expressing cells is GPI dependent and sialic acid independent (abstract). Conversely, NgR binds to MAG-expressing cells. MAG, but not a truncated MAG, binds neurons, but does not inhibit regeneration, and precipitates NgR from NgR-expressing cells and cerebellar neurons (abstract). NgR antibody, soluble NgR, or dominant-negative NgR each prevent inhibition of neurite outgrowth by MAG. Also, MAG and Nogo66 compete for binding to NgR. The results by Domeniconi et al., suggest redundancy in myelin inhibitors and indicate therapies for CNS injuries (abstract).

The specification discloses that the three NgRs (NgR1 [also called NgR] (473 residues), NgR2 (420 residues), and NgR3 (445 residues)) share identical domain organization (p. 2, lines 5-7). The NgRs also show distinct binding preferences for the myelin inhibitors Nogo-66, MAG, and OMgp (p. 3, lines 23-24). Conversely, Nogo-66, MAG-Fc, and OMgp show overlapping, but distinct binding to the NgRs (p. 3, line 29). The specification, which is somewhat in conflict with the art, teaches that Nogo-66 binds NgR1, but not NgR2 or NgR3. MAG-Fc binds NgR1 and NgR2 (with high affinity), but not NgR3. OMgp binds NgR1, but not NgR2 and NgR3 (p. 3, lines 30-32).

Claim 38 reads on a genus of chimeric fusion proteins comprising all of NgR1 and the "MAG binding motif of NgR2." The sequence comprising the "MAG binding motif of NgR2" is not clearly taught in the specification or the art such that the person of skill in the art would readily understand which sequence or region Applicant is referring to. The specification states that introducing the 13-amino acid NgR2 peptide (Pro315-Ser 327) juxtaposed to the NgR1-LBD domain (residues 1-314) is sufficient to convert NgR1 into a high affinity MAG binding receptor while maintaining Nogo66 and OMgb binding capacity (p. 6, lines 28-30). This is called "NgR^{OMNI}" in the instant specification (p. 6, line 30). The specification states that a mutation of N325E in NgR^{OMNI} greatly reduced MAG binding (p. 6, line 31). In support of residues 315-327 of the NgR2 polypeptide being the "MAG binding motif" sequence, the specification teaches that NgR2 (residues 315-420) [called "NgR2-unique"] fused to NgR1-LBD (residues 1-314) are sufficient to support high affinity MAG binding (p. 6, lines 22-23). However, this same NgR2-unique domain (which contains residues 315-327 of NgR2) fused to residues 1-309 of NgR3 does not support MAG binding (p. 6, lines 24-25). If residues 315-420 are sufficient to support MAG binding in one case, but not another, it is uncertain how this region can be considered a "MAG binding motif." Additionally, NgR1 (residues 1-353) fused to NgR2 (residues 328-420) are not sufficient to support high affinity MAG binding (p. 6, lines 26-28). Thus, it appears residues 328-420 of NgR2 are not sufficient to be deemed a "MAG binding motif" by themselves. Strangely, when the fusion chimera is oriented completely the opposite direction with a C-terminal NgR2 domain and an N-terminal domain from NgR1 [NgR2-LBD (residues 1-315) fused to NgR1 (residues 313-473)] the construct weakly binds MAG (p. 96, lines 30-32). This is confusing because the C-terminal NgR2 construct is oriented in such a way that it does not contain the putative "MAG binding motif" (residues 315-327 of NgR2) at all. The guidance in the specification is lacking as to which portion of NgR2 actually has MAG binding ability such that one of skill in the art would reasonably understand which part, sequence, region, or domain of NgR2 comprises the "MAG binding motif." The examples demonstrate that multiple parts of NgR2 have

MAG binding ability in some cases, but not in others. There is no explanation in the specification for the lack of predictability in determining the structure of a "MAG binding motif."

The specification also teaches that NgR2 supports high affinity binding of MAG (p. 6, line 19) and that NgR2 sequences (residues 315-327) juxtaposed to the NgR2-LBD are necessary for high affinity MAG binding (p. 6, lines 25-26). However, there is insufficient guidance in the specification that residues 315-327 of NgR2 alone are sufficient to comprise a "MAG binding motif" when these residues are part "NgR2-unique" that bound MAG as a chimera comprising NgR1-LBD (residues 1-314) fused to NgR2 (residues 315-420), but did not bind MAG as a NgR3 (residues 1-309) fused to NgR2 (residues 315-420). The specification also teaches that the NgR1 C-terminal domain is necessary to signal myelin inhibition (p. 5, lines 30-31; Figure 9). There is no guidance in the specification as to which part of the C-terminal domain of NgR1 is required to signal myelin inhibition and whether this is the cause of conflicting experimental results of why the "NgR2 unique" region bound MAG when fused to NgR1 (residues 1-314) but not when fused to NgR2 (residues 1-309).

Additionally, claim 38, as written, is not limited to how much or how little of the NgR1 protein one would have to include in the chimera in order to have a functional chimera fusion protein. The specification teaches that the NgR1 c-terminal domain is necessary to signal myelin inhibition (p.5, lines 30-31). However, claim 38 does not require the C-terminal domain of NgR1 in the claimed genus of chimeras and no function is set forth in claim 38 to require the chimera to have the biological function of myelin inhibition. Further, claim 38 does not limit the "MAG binding motif" of NgR2 to any particular NgR2 sequence, region, or domain. When read in its broadest reasonable interpretation, claim 38 reads on a chimera comprising all of NgR1 plus NgR2 or any part thereof. Further, because the NgR2 "unique domain" (residues 315-420) does not appear to bind MAG on its own (t was unable to bind MAG when fused to the NgR3-LBD domain (residues 1-309) (see spec p. 6, lines 24-25)), it is not clear that residues 315-420 of NgR2 comprise a MAG binding domain. As such, it would require undue experimentation for a person of skill in the art to make and test a sufficient number of NgR1-NgR2 chimera fusion proteins and test the same for activity. Applicant has clearly demonstrated the unpredictability of a generic NgR1-NgR2 chimera fusion to bind MAG. The specification does not sufficiently teach the structure of the genus of chimeric fusion proteins comprising NgR1 and the NgR2 "MAG binding motif" such that the structure of the "MAG binding motif" may be correlated with the function of binding MAG.

Applicant teaches several variations of chimeric NgR1/NgR2-"MAG binding motif" fusion proteins. However, the instant claims, as written, do not require MAG binding as a function. Rather, the claims are silent as to any biological function of the claimed genus of chimeras. However, MAG binding

is taught in the specification as the primary indicator of functional activity of the exemplary chimeric fusion proteins. It would be unpredictable for a person of skill in the art to make the genus of chimeric NgR1/NgR2-"MAG binding motif" fusion proteins without knowing whether they are functional or understanding how to distinguish a chimera comprising a NgR2 "MAG binding motif" if the chimera is not required to bind MAG. There is no guidance provided on how to use the NgR1/NgR2 "MAG binding motif" chimeric fusion proteins in the absence of their ability to bind MAG. It is noted that the claims, as written, encompass non-functional embodiments, weakly functional embodiments, highly functional embodiments, and every variation in between.

With regard to claim 41, the wild type NgR1 and NgR1 receptors are taught in both soluble and membrane bound forms (p. 61, Example 1, subpart (1)). However, because claim 41 depends from claim 38 and the "MAG binding motif" of NgR2 (see claim 38) cannot be predictably ascertained (see discussion above), one of skill in the art would not be able to predict whether any given chimeric NgR1 and NgR2 "MAG binding motif" construct would be soluble. The person of skill in the art would be required to make and test a sufficient number of variants and test the same in order to determine whether the configuration was soluble or insoluble. This would require undue experimentation in light of the fact that the structure of the "MAG binding motif" is not clearly defined in the specification or by the art.

With regard to the methods of claims 50 and 51, which both recite the use of the chimera fusion protein of claim 38, the person of skill in the art would not understand how to use a protein that has no recited function. Because the genus of chimeric fusion proteins of claim 38 is not limited to functional embodiments, one of skill in the art would not know how to use a generic chimeric fusion protein in a method of modulating myelin inhibitor activity (claim 50) or in a method of treating a central nervous system disorder (claim 51). The specification states that it discloses methods of treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of a chimeric NgR protein comprising the MAG binding motif of NgR2. "Optionally, the chimera comprises amino acids 1-314 of NgR1 and 315-327 of NgR2, and 354-473 of NgR1 (SEQ ID NO: 21)…the chimera of the method can be in soluble or membrane bound form" (p. 45, lines 20-25). The method of treating a central nervous system disorder is set forth in virtually identical language on p. 46, lines 16-21. However, there are no working examples of *in vivo* administration or treatment using one or more of the claimed chimeric fusion proteins. Although working examples are not required, they are helpful in determining whether Applicant has sufficiently taught how to make and use the invention within its full scope. In the instant case, because the genus of chimeric fusion proteins of claim 38 recites a non-specific NgR2 "MAG binding domain" (discussed above) and because no function is recited for the genus of chimeric

fusion proteins, the specification has not provided sufficient guidance to teach one of skill in the art how to use the chimeric fusion proteins in a method of modulating myelin inhibitor activity or a method of treating central nervous system disorders.

Additionally, the phrase "myelin-derived-growth-inhibitory protein" in claim 50 is not defined or otherwise limited in the specification. The specification discloses that the phrase includes the ligands Nogo, MAG, and OMgp (p, 16, lines 2-4). However, the recitation of only three ligands is insufficient to provide sufficient guidance on what a "myelin-derived-growth-inhibitory protein" is supposed to be. One of skill in the art would not be able to predictably determine what a "myelin-derived-growth-inhibitory protein" is without undue experimentation.

Due to the large quantity of experimentation necessary to determine the "MAG binding motif" of NgR2, the lack of direction/guidance presented in the specification regarding same, the absence of sufficient working examples directed to same, the complex nature of the invention, the state of the prior art establishing that wild type NgR1 and NgR2 both bind MAG along with the conflicting experimental data in the specification showing that the identical regions of NgR2 bind and fail to bind MAG when expressed with different C-terminal constructs or that the C-terminal region of NgR2 and N-terminal region of NgR1 (opposite in orientation from the majority of examples set forth as the "MAG binding motif") actually binds MAG, albeit weakly, and the breadth of the claims which fail to recite a specific region, domain, or sequence for the "MAG binding motif" of NgR2, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 38, 41, 50, and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1

"Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to a genus of chimeric NgR1 proteins comprising the "MAG binding motif" of NgR2; wherein the chimeric protein is soluble; a method of modulating myelin inhibitor activity comprising contacting a myelin-derived-inhibitor protein with the chimera; a method of treating a central nervous system disorder in a subject comprising administering to the subject an effective amount of the chimera.

Vas-Cath Inc. V. Mahurkar, *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111, (Fed. Cir. 1991), states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e., a genus of chimeric NgR1 fusion proteins comprising the MAG binding motif of NgR2.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states, "An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention."

There are functional individual species of the claimed genus disclosed that are within the scope of the claimed genus, *i.e.* SEQ ID NO: 21, NgR2 (residues 315-420) [called "NgR2-unique"] fused to

NgR1-LBD (residues 1-314), and NgR2-LBD (residues 1-315) fused to NgR1 (residues 313-473). The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described.

Claim 38 reads on a genus of chimera proteins comprising all of NgR1 and the "MAG binding motif of NgR2." The sequence comprising the "MAG binding motif of NgR2" is not clearly described in the specification or the art such that the person of skill in the art would readily understand the sequence or region Applicant is referring to. The specification states that introducing the 13-amino acid NgR2 peptide (Pro315-Ser 327) juxtaposed to the NgR1-LBD domain (residues 1-314) is sufficient to convert NgR1 into a high affinity MAG binding receptor while maintaining Nogo66 and OMgb binding capacity (p. 6, lines 28-30). This is called "NgR^{OMNI}" in the instant specification (p. 6, line 30). The specification states that a mutation of N325E in NgR^{OMNI} greatly reduced MAG binding (p. 6, line 31). In support of residues 315-327 of the NgR2 polypeptide being the "MAG binding motif" sequence, the specification teaches that NgR2 (residues 315-420) [called "NgR2-unique"] fused to NgR1-LBD (residues 1-314) are sufficient to support high affinity MAG binding (p. 6, lines 22-23). However, this same NgR2-unique domain (which contains residues 315-327 of NgR2) fused to residues 1-309 of NgR3 does not support MAG binding (p. 6, lines 24-25). If residues 315-420 are sufficient to support MAG binding in one case, but not another, it is uncertain how this region can be considered a "MAG binding motif." Additionally, NgR1 (residues 1-353) fused to NgR2 (residues 328-420) are not sufficient to support high affinity MAG binding (p. 6, lines 26-28). Thus, it appears residues 328-420 of NgR2 are not sufficient to be deemed a "MAG binding motif" by themselves. Strangely, when the fusion chimera is oriented completely the opposite direction with a C-terminal NgR2 domain and an N-terminal domain from NgR1 [NgR2-LBD (residues 1-315) fused to NgR1 (residues 313-473)] the construct weakly binds MAG (p. 96, lines 30-32). This is confusing because the C-terminal NgR2 construct is oriented in such a way that it does not contain the putative "MAG binding motif" (residues 315-327 of NgR2) at all. The specification is lacking a clear description of which portion of NgR2 actually has MAG binding ability, such that one of skill in the art would reasonably understand which part, sequence, region, or domain of NgR2 comprises the "MAG binding motif." The examples demonstrate that multiple parts of NgR2 have MAG binding ability in some cases, but not in others. There is no explanation in the specification for the lack of disclosure as to the structure of the "MAG binding motif."

With regard to claims 50 and 51, they recite a method of modulating myelin inhibitor activity (claim 50) and a method of treating a central nervous system disorder (claim 51). However, the

specification does not sufficiently describe the structure of the genus of chimeric fusion proteins comprising NgR1 and the NgR2 "MAG binding motif" such that the structure of the "MAG binding motif" may be correlated with the function of binding MAG. Because the genus of chimeric fusion proteins of claim 38 recites a non-specific NgR2 "MAG binding domain" (discussed above) and because no function is recited for the genus of chimeric fusion proteins, the specification has not provided a sufficient disclosure to substantiate a structure for the genus of chimeric fusion proteins to be used in the recited methods. The lack of a defined "MAG binding motif" structure mitigates against Applicant's possession of the full scope of the genus of chimeric fusion proteins, as claimed, at time the application was filed.

While "examples explicitly covering the full scope of the claim language" typically will not be required, a sufficient number of representative species must be included to "demonstrate that the patentee possessed the full scope of the [claimed] invention." Lizardtech v. Earth Resource Mapping, Inc., 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is a genus of chimeric NgR1 fusion proteins comprising the MAG binding motif of NgR2. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features (see, Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 927, 69 USPQ2d 1886, 1895 (Fed. Cir. 2004); accord Ex Parte Kubin, 2007-0819, BPAI 31 May 2007, opinion at p. 16, paragraph 1). The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, Second Paragraph

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 38-41, 50, and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 recites a chimeric NgR1 protein comprising the MAG binding motif of NgR2. In the absence of an alternative definition, an "NgR1 protein" would read on the whole protein and not a fragment thereof. Claim 38 is written in such a way that it literally recites the whole NgR1 protein also comprising the MAG binding domain of NgR2. Using a literal interpretation of claim 38, one of skill in the art would understand that the "chimera" would comprise all of NgR1 with the MAG binding motif of NgR2 added to either the C-terminal or the N-terminal of the NgR1 protein or inserted at any point into the NgR1 sequence. However, this literal recitation does not appear to be what applicant intends the invention to be, as evidenced by the chimera of claim 39, which recites only certain regions or fragments of NgR1 and also comprises part of NgR2 positioned in the middle of the various NgR1 fragments. None of the exemplified chimeras in the specification read on the entire NgR1 protein as literally recited in claim 38; none of them comprise the full length NgR1 with the NgR2 MAG binding motif at either the C-terminal or the N-terminal and none of them comprise the full length NgR1 with the NgR2 MAG binding motif inserted at any point into the full NgR1 sequence.

The metes and bounds of what constitutes a chimeric NgR1 protein, apart from the entire protein, are not disclosed or sufficiently distinguished in the specification such that one of ordinary skill in the art would understand that Applicant's invention was drawn to a chimera comprising only a fragment of NgR1, as set forth in dependent claims 39 and 40, or in the various examples in the specification (see detailed discussion above). The specification fails to set forth what structure defines a polypeptide such that it is an NgR1 protein other than the full length sequence. For example, amino acids 23-231 might define a structure which confers NgR1-ness to a polypeptide such that any polypeptide comprising amino acids 23-231 would be considered an NgR1 polypeptide. However, such an example or other definition is absent from the specification. Moreover, claim 38 is vague and indefinite because Applicant intends fragments of NgR1 to be encompassed in the claimed genus of chimeras. Applicant has not set forth the structure of what constitutes an "NgR1 protein" such that one of skill in the art would understand that by reciting an "NgR1 protein" Applicant only means an NgR1 fragment.

Although claim 38 is written in such a way that it reads on the entire NgR1 protein also comprising the MAG binding motif of NgR2, the examiner has also considered the teachings in the specification and the dependent claims which read on chimeras comprising less than all of NgR1. Claims 39-41 and 50-51 are rejected because of their dependency on a rejected claim.

Conclusion

NO CLAIM IS ALLOWED.

SEQ ID NO: 21 is free of the prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:00am-5:30pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Cherie M. Woodward/
Examiner, Art Unit 1647